European Journal of Vascular and Endovascular Surgery 43 (2012) 466–471

Contents lists available at SciVerse ScienceDirect

European Journal of Vascular and Endovascular Surgery

journal homepage: www.ejves.com

SUPERvised Exercise Therapy or Immediate PTA for Intermittent Claudication in Patients with an Iliac Artery Obstruction – A Multicentre Randomised Controlled Trial; SUPER Study Design and Rationale

F.A. Frans [a], S. Bipat [a], J.A. Reekers [a], D.A. Legemate [a], M.J.W. Koelemay*,[a], on Behalf of the SUPER Study Collaborators

Academic Medical Center, Meibergdreef 9, 1105 AZ, Amsterdam, The Netherlands

WHAT THIS PAPER ADDS

- We present the design and rationale of the recently initiated SUPER study, a multicentre randomised controlled trial on supervised exercise therapy or immediate PTA for intermittent claudication in patients with an iliac artery obstruction. Intermittent claudication is a common and disabling condition and there still is no consensus regarding the most optimal treatment for this large and heterogeneous patient population. With this study we hope to influence future clinical practice and eventually provide a clinical and cost-effective package of care for intermittent claudication in patients with an iliac artery obstruction.

ARTICLE INFO

Article history:
Received 7 November 2011
Accepted 13 January 2012
Available online 10 February 2012

Keywords:
Peripheral arterial disease
Intermittent claudication
Angioplasty
Exercise

ABSTRACT

Introduction: Treatment of intermittent claudication (IC) due to peripheral arterial disease (PAD) is aimed at improving walking distance and includes secondary prevention of cardiovascular disease. Both supervised exercise therapy (SET) and percutaneous transluminal angioplasty (PTA) have proven to be effective in increasing maximum and pain-free walking distance in IC. However, the optimal treatment strategy in patients with IC due to iliac artery stenosis or occlusion remains unclear.
Objective: To compare the (cost-) effectiveness of initial PTA versus initial SET in patients with disabling IC due to an iliac artery obstruction.
Design: In a multicentre randomised controlled trial 400 consecutive patients with IC will be randomly assigned to PTA (with additional stent placement on indication) or SET. Primary outcomes are maximum walking distance and health-related quality of life measured using the disease-specific VascuQol instrument after 1 year. Secondary outcomes are pain-free walking distance, functional status, generic quality of life, complications related to each of the interventions, additional interventions, treatment failures and costs (cost-effectiveness and cost-utility) after 1 year.
Conclusion and implications: Based on the results of this proposed large study well-founded adjustments of existing guidelines on the treatment of iliac artery occlusive disease can be implemented (Clinical Trials.gov NCT01385774; Nederlands Trial Register NTR2776).

Treatment of patients with intermittent claudication (IC) is aimed at increasing pain-free walking distance and subsequently quality of life (Qol). Treatment also includes secondary prevention of cardiovascular events by controlling risk factors for atherosclerosis. Exercise programmes, percutaneous transluminal angioplasty (PTA), drugs and surgery can effectively relieve IC.[1–4] Currently, the most frequently applied therapies for IC are exercise programmes and PTA.[4,5]

A systematic review of eight randomised controlled trials (RCTs) comparing both supervised and unsupervised exercise therapies ((S)ET) with PTA was unable to demonstrate the superiority of one particular therapy with regard to walking distance and Qol. This review included 702 patients with IC due to both aortoiliac and femoropopliteal artery disease.[6] The implications for patient

* Corresponding author. Tel.: +31 20 5666654; fax: +31 20 5669432.
E-mail address: m.j.koelemaij@amc.uva.nl (M.J.W. Koelemay).
[a] SUPER study investigators and collaborators (Members listed in Appendix).

1078-5884/$ – see front matter © 2012 European Society for Vascular Surgery. Published by Elsevier Ltd. All rights reserved.
doi:10.1016/j.ejvs.2012.01.014

management based on this systematic review are unclear, as most studies do not specify the degree of arterial obstruction. PTA of an iliac artery obstruction is an attractive and effective treatment with 4-year patency rates of 70%.[4] SET can also effectively improve pain-free walking distance,[7,8] but specifically in patients with iliac artery stenosis or occlusion the benefit of SET is unclear. The only published high-quality RCT included 106 patients with an iliac artery obstruction and could not demonstrate a difference in effectiveness between PTA and SET, possibly because the study was underpowered.[9,10] Thus, the optimal treatment strategy of patients with IC due to an iliac artery obstruction still needs to be defined.

The objective of the SUPER study is to compare the clinical effectiveness and the cost-effectiveness of SET and PTA as treatment for IC due to an iliac artery obstruction. We hypothesise that first-line treatment with PTA is more effective than SET with regard to maximum walking distance (MWD), Qol and costs after 1 year.

Methods

Setting

SUPER study is a multicentre randomised controlled trial and will be conducted in 15 Dutch hospitals and their allied local physiotherapy practices. The study aims to include 400 consecutive outpatients with IC who are able to walk a distance of between 100 and 300 m on a treadmill at 3.2 km h^{-1} and 10% incline. All patients must have an iliac artery obstruction with a diameter reduction $\geq$50% as assessed by colour duplex scanning (CDS), magnetic resonance angiography (MRA) or computed tomography angiography (CTA). Usually, patients are referred by a general practitioner to the participating hospital where they are further evaluated by a vascular surgeon. A concomitant >50% stenosis or occlusion in the superficial femoral artery (SFA) is not a contraindication to inclusion. For all inclusion and exclusion criteria, see Fig. 1. The final results of the trial will be reported in line with the CONSORT (CONsolidated Standards of Reporting Trials) statement.[11]

Ethics and informed consent

The study will be conducted according to the principles of the Declaration of Helsinki (World Medical Association Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects Version Edinburgh, Scotland, October 2000), with Note of Clarification on Paragraph 29 added by the WMA General Assembly, Washington 2002 end Note of Clarification on Paragraph 30 added by the WMA General Assembly, Seoul 2008 and in accordance with the Medical Research Involving Human Subjects Act (WMO) and other guidelines, regulations and Acts.[12] Patients can only participate in the study when they fulfil the inclusion criteria and give written informed consent. The study has been approved by the Medical Ethical Committee at the Academic Medical Center, Amsterdam (MEC 09/285). The SUPER study is registered under Trial registration NTR2776 and NCT01385774.[13,14]

Treatment groups

Participating patients will be randomly allocated to SET or PTA.

SET group

SET will be either hospital-based or community-based in accordance with the guidelines of the Royal Dutch Society for Physiotherapists.[15] SET will be given for 6 months. It will start with a frequency of 2 times a week for 12 weeks, then once a week for 8

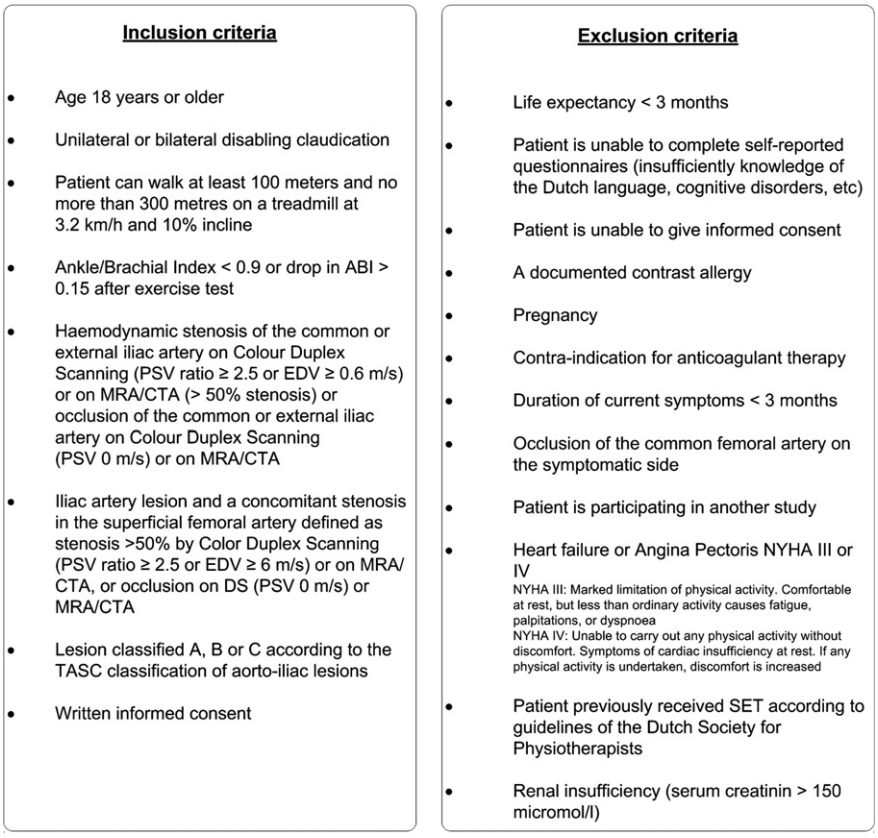

Figure 1. Eligibility criteria.

weeks and finally once every 2 weeks for 4 weeks. After 6 months, patients are regarded sufficiently trained and will perform the training on their own. Compliance to SET is recorded by the physiotherapist (PT) at 1, 3 and 6 months. Furthermore, we will ask the patients at the 12 months' follow-up visit if they have had SET by a PT between 6 and 12 months.

A well-designed SUPER study SET programme has been created. The summary of this programme is shown in Fig. 2. The SET programme is sent in advance to each PT practice, who will train a SUPER study patient. We will refer each SUPER study patient only to a dedicated trained PT, who is able to offer SET according to the SUPER study SET programme. In addition, we will perform visits and interviews with the PT practices to check if the programme is indeed executed.

PTA group

The PTA procedure will be performed by an experienced interventional radiologist. An experienced radiologist is officially registered with and certified by the Dutch society of Interventional Radiology. An additional stent will be placed if the residual mean pressure gradient is greater than 10 mmHg across the treated site or in case of a residual stenosis of more than 30%, which is considered a poor initial result.[16,17] All PTA patients will be encouraged to undertake at least three walking sessions every day.

Cardiovascular risk factor management and background therapy

In accordance with the Dutch guideline "Diagnosis and treatment of peripheral arterial disease of the lower extremity,"[18] irrespective of cholesterol levels, all patients will receive a statin, antiplatelet therapy (aspirin 100 mg) and, if necessary, blood pressure-lowering therapy (targets 140/90 mmHg and 130/80 mmHg in diabetics). Patients will be advised to stop smoking.

Co-intervention

If, after a minimum of 6 months, IC continues to be persistent and disabling in patients allocated to SET, a delayed PTA may be carried out. Also, if persistent disabling IC continues after initial PTA, the patient may be referred for additional SET. Persistent disabling IC is defined as persisting symptoms perceived by the patient. Delayed PTA or additional SET will be considered as treatment failure.

Randomisation

Randomisation will be computer- and web-based using stratification to ensure a balanced distribution of known possible confounders in both treatment groups, and in blocks of variable size. Randomisation will be stratified according to the following characteristics: MWD at baseline (less or more than 200 m), and concomitant SFA stenosis or occlusion. To ensure allocation concealment the randomisation list has been generated using an online computer software program (ALEA NKI-AVL, Amsterdam, The Netherlands, Release: 2.2.) and implemented into the web-based application.

Assessments

Fig. 3 shows the timeline of patient inclusion and follow-up with accompanying assessments. Follow-up assessments are scheduled at 1, 6 and 12 months after start of treatment, SET or PTA.

- At baseline and follow-up visits pain-free and MWD will be assessed using a treadmill test which, in accordance with the Trans Atlantic Inter-Society Consensus (TASC) guidelines, is set at 3.2 km h^{-1} and 10% incline.[3] At follow-up visits (at 1, 6 and 12 months) the treadmill test will be recorded by an observer who is blinded to treatment allocation. For logistical reasons the MWD will be set at 800 m, equivalent to 15 min on the treadmill, at the three follow-up assessments.
- The ankle–brachial index (ABI), defined as the ratio of the highest systolic pressure of the dorsal pedal and posterior tibial arteries divided by the highest of both brachial systolic pressures,[19] will be measured at rest and after the treadmill test.
- CDS, MRA or CTA will be used to grade patency of the iliac artery in patients allocated to the PTA group after 12 months.
- Health-related Qol and functional outcome questionnaires will be used to measure patient-centred outcomes such as ambulatory status, activities of daily life (ADL), independence and perceived psychosocial well-being.[20,21] For health-related QoL, both generic Qol, using EQ-5D and Short Form 36 (SF-36)[22] questionnaires and disease-specific Qol, using the Vascular Quality of Life (VascuQol) questionnaire, will be used.[23–25] Generic scales are less sensitive in detecting subtle changes in Qol.
- Functional outcome will be evaluated by the AMC Linear Disability Score (ALDS). The ALDS is a generic item bank used to assess the level of ADL in patients with chronic disease.[26] The ALDS item bank contains 77 items covering a wide scale of daily activities. From the item bank, clinicians can select the items that are most applicable to the population that they are investigating ('best' items). Based on clinical relevance and adapted to the disability level of this specific patient group, 28 items have been selected for the current study. The scores range from 0 to 100 and lower scores correspond with a higher level of disability. Previous evaluation of ALDS in patients in

- The physiotherapist informs the patient about the training and the importance of day to day exercise.
- The physiotherapist records the personal walking speed of the patient on a 6-minute walking test.

- The duration of each session is 60 minutes.
- During the first 30 minutes the patient walks on a treadmill to the ACSM (American College of Sports Medicine) Claudication Pain Rating Scale 3 (Intense Pain) as many times as possible.
- During the second 30 minutes, the training focuses on walking pattern improvement and enhancement of endurance and strength. This is tailored to the individual physiotherapy practice, and the individual needs of the patient.

- All patients receive homework, make a plan and keep a log of their exercise activities.
- The homework includes goals to enhance day-to-day exercise according to the patient's own preferences, e.g. walking to the shops or in the park.
- The patient receives feedback by doing a graded treadmill test (increasing slope of 2% every 2 minutes) every 4 weeks.
- Additionally, besides coaching and monitoring the patient's homework, the physiotherapist advises on coping and problems encountered during homework and day-to-day exercise.

Figure 2. Description of Supervised Exercise Therapy (SET).

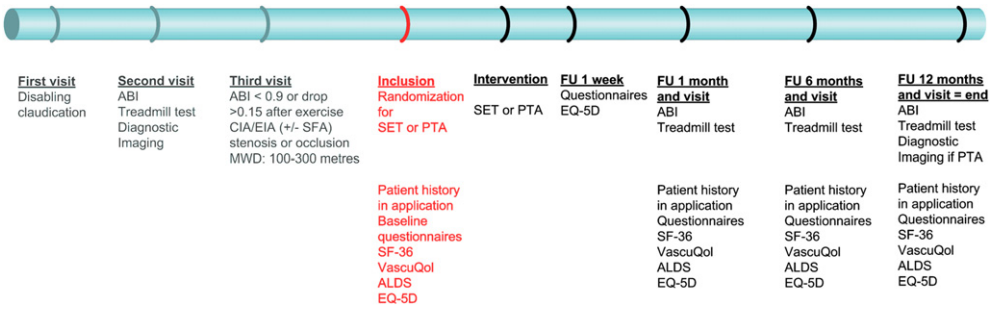

Figure 3. Timeline SUPER study.

various stages of peripheral arterial disease has shown good internal reliability, consistency and correlation with the activity domain of the VascuQol.[27,28] All four questionnaires (EQ-5D, SF-36, VascuQol and ALDS) will be recorded at baseline, 1, 6 and 12 months' follow-up. The EQ-5D will also be completed at 1-week follow-up.

Outcomes

Primary outcomes are MWD on a standardised treadmill test at a speed of 3.2 km h^{-1} at 10% incline, and Qol measured using the disease-specific VascuQol instrument after 1 year.

Secondary outcomes are pain-free walking distance on the treadmill, functional status as assessed by the AMC Linear Disability Score (ALDS), generic Qol measured with the SF-36 and EQ-5D, complications related to both interventions, treatment failures (defined as crossover to the other treatment arm), additional interventions and costs after 1 year (Fig. 4).

Analysis

Analysis is carried out according to the intention-to-treat principle. Baseline characteristics are summarised using descriptive statistics. Differences in MWD and Qol at 12 months between the treatment groups will be compared with a two-tailed unpaired *t*-test, and, if necessary, multiple linear regression to take into account unbalanced baseline values of the VascuQol and treadmill test. Additionally, the repeated data structure of both primary outcomes is analysed using a mixed linear model.

For comparisons of the secondary outcomes, depending on the distribution of data the χ^2-test or Fisher's exact test, unpaired *t*-test or Mann–Whitney test are used. In all analyses, statistical uncertainties are expressed in 95% confidence intervals and *p*-values <0.05 will indicate statistical significance.

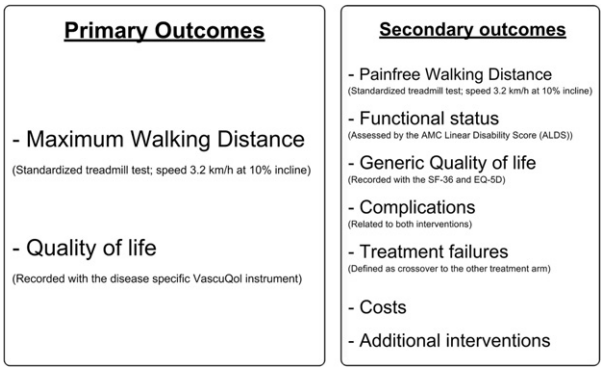

Figure 4. Primary and secondary outcomes after one year.

Sample size

Since little is known about the expected treatment effect that will be revealed on the continuous VascuQol scale, Cohen's effect size *d* is used as the benchmark to assess the relative magnitude of score differences between each of the treatment groups. We assume a moderate effect ($d = 0.4$) on Qol and MWD. A sample size of 180 patients in each group has 90% power to detect a difference in VascuQol score means of 0.377 between the SET and the PTA group, at a two-sided significance level of 5% (assuming overall VascuQol scores of 4600 and 4977 (common standard deviation (SD) 1.1), respectively).

Using an unpaired *t*-test with a 0.05 two-sided significance level, this sample size also has 90% power to detect a difference in means of 86 m MWD on a treadmill at a speed of 3.2 km h^{-1} at 10% incline (SET group mean of 250 m and the PTA group mean of 336 m) assuming a common SD of 250 m. Anticipating a maximum dropout rate of 10%, 200 patients need to be included in each treatment arm.

Cost-effectiveness analysis

The economic evaluation of PTA versus SET will be performed from a societal perspective as a cost-effectiveness analysis with the costs per patient able to walk 250 m at a speed of 3.2 km h^{-1} with a 10% incline as a primary outcome measure.

Additionally, a cost-utility analysis will be carried out with the costs per quality adjusted life-year (QALY) as outcome. The EQ-5D is used to generate health status scoring profiles over time, which will subsequently be translated into QALYs by applying time trade-off-based health-utility algorithms and assuming that interpolation between successive measurements best reflects a patient's health status during the year.[29,30]

The time horizon for the cost-effectiveness as well as cost-utility analysis is 1 year.

The evaluation will include the direct medical costs, out-of-pocket expenses and the indirect non-medical costs of productivity losses. Volume data will be gathered with clinical report forms, available hospital information systems and the Dutch Health and Labour Questionnaire adapted for this patient population (to be completed at baseline, and at months 1, 6 and 12). Unit costing will comply with the Dutch costing manual for health-care research. After price-indexing all costs will be expressed in euros for the base year 2011.

The sample size of 400 patients (accounting for 10% dropout) is sufficient to detect clinically relevant differences in QALYs based on the EQ-5D, which is a generic health status measure that is less sensitive than the disease-specific VascuQol. Starting at a baseline health utility level of about 0.69 (SD 0.2) in the study population,[10] we expect a 10% improvement in the SET arm, resulting in a health utility of 0.759 following treatment. A clinically relevant difference

favouring PTA over SET would be a doubling of such an improvement (i.e., by 20%). Given the follow-up duration of 12 months, the sample size of 180 patients per group has 90% power to detect a difference in means of 0.069 in QALYs (SET group mean of 0.759 QALY and the PTA group mean of 0.828 QALY) assuming a common SD of 0.2 QALY and using a 0.05 two-sided significance level.

Safety monitoring

To ensure the safety of each study subject a Data Safety Monitoring Committee (DSMC) has been established. The DSMC will not only advise the SUPER study investigators regarding the continuing safety of study participants but also ensure the integrity of the study conduct and results, provide an independent review of safety and will review the formal safety analysis. Two interim analyses of safety are planned for this study.

Safety analysis

There is no formal safety stopping guideline for this study, since both treatments are standard clinical care. The DSMC may recommend stopping the study at any time for significant safety issues. The DSMC may also recommend an unplanned interim analysis due to safety concerns.

Other considerations

In our systematic review, we found no evidence for the superiority of any combination of SET and PTA over another. Yet, it is common practice to refer a patient with IC and an iliac obstruction for a PTA and not SET. The aim of our study is therefore to compare the relative effectiveness of both treatments. It would be relevant to compare other combinations, such as SET versus SET and PTA, or PTA versus SET and PTA, as such studies will determine the additional value of the combination of interventions over a single intervention. We know that a third study arm with a combination strategy with PTA and SET would provide more answers, but due to logistic reasons, costs and the fact that a much larger sample size would be needed to detect clinically relevant differences we decided to restrict the study to a head-to-head comparison of PTA and SET.

Conclusion and Implications

As multiple vascular specialists are involved in the care of patients with intermittent claudication, knowledge transfer is primarily aimed at these health-care professionals. The results of this study will contribute to existing guidelines on the treatment of iliac artery occlusive disease. Implementation of the results and guidelines will be facilitated by the broad network of participating hospitals (a wide spectrum of institutions including academic and teaching hospitals), and allied physiotherapy practices.

This study will be the largest RCT on this subject to be carried out so far and the impact of the findings will therefore be substantial, from both a practical and a scientific point of view. The official SUPER study inclusion will start in September 2011. With an inclusion period of 2 years and 1-year follow-up, the first results are expected by the end of 2014.

Appendix

SUPER Study Investigators

(Frans FA [Department of Surgery and Radiology], Bipat S [Department of Radiology], Reekers JA [Department of Radiology], Legemate DA [Department of Surgery], Koelemay MJW [Department of Surgery] Academic Medical Centre Amsterdam).

SUPER Study collaborators

(Dijkgraaf MGW [Clinical Research Unit], De Haan RJ [Clinical Research Unit] Academic Medical Center Amsterdam); (Engelbert RHH, Van Egmond MA, Poelgeest A [Department of Rehabilitation, Amsterdam Medical Center, Amsterdam and University of Applied Sciences, Education of Physiotherapy, Amsterdam]); (Geleijn E [Department of Physiotherapy] VU Medical Center Amsterdam); (van der Voort SSEM, Honing B [Department of Physiotherapy]; Tergooiziekenhuizen Hilversum en Blaricum).

(De Vries JPPM [Department of Surgery], Vos JA [Department of Radiology]; Sint Antonius Ziekenhuis Nieuwegein), (De Nie AJ [Department of Surgery], Kamphuis A [Department of Radiology]; Rode Kruis Ziekenhuis Beverwijk), (Vahl AC [Department of Surgery], Montauban van Swijndregt AD [Department of Radiology]; Onze Lieve Vrouwe Gasthuis Amsterdam), (Vermeulen EGJ [Department of Surgery], Van Kelckhoven BJ [Department of Radiology]; Kennemer Gasthuis Haarlem), (Van der Vliet JA [Department of Surgery], Schultzekool LJ [Department of Radiology]; University Medical Centre Nijmegen St. Radboud), (Willems M [Department of Surgery], De Bruine JHD [Department of Radiology]; Flevoziekenhuis Almere), (Hoksbergen A [Department of Surgery], Lely R[Department of Radiology]; VU Medical Centre Amsterdam), (Hollander EJF [Department of Surgery], Pels Rijcken T [Department of Radiology]; Tergooiziekenhuizen Hilversum en Blaricum), (Buscher HCJL [Department of Surgery], Slis HW [Department of Radiology]; Gelre Ziekenhuizen Apeldoorn), (Elsman BHP[Department of Surgery]; Aarts JCNM[Department of Radiology]); Deventer Ziekenhuis), (Reijnen MMPJ [Department of Surgery]; van Oostayen JA [Department of Radiology], Rijnstate Hospital Arnhem), (Van Nieuwenhuizen RC [Department of Surgery], Wüst AFJ [Department of Radiology]; Sint Lucas Andreas Ziekenhuis Amsterdam),(Nio D [Department of Surgery], van de Rest HJM [Department of Radiology]; Spaarne Ziekenhuis Hoofddorp), (Van den Broek ThAA [Department of Surgery]; Moolhuijzen A [Department of Radiology]; Waterland Ziekenhuis Purmerend)

Data Safety Monitoring Committee

Chair: Buskens CJ [Department of Surgery], Academic Medical Centre Amsterdam

Voting Members: (Zeebregts CJ [Department of Surgery], University Medical Centre Groningen), (de Bie RA [Department of Epidemiology & Institute for Education], Maastricht University Medical Centre), (van Overhagen H [Department of Radiology] Hagahospital, The Hague).

Author Contributions

The SUPER Study Investigators FAF, MJWK and SB wrote the first draft of the manuscript. JAR and DAL contributed to the completion of the manuscript. All the authors listed as the writing committee made substantial contributions to the conception and design of the study, and also contributed to drafting the article or revising it critically for important intellectual content. The collaborators (local investigators) listed at participating centres all revised the manuscript critically and will make contributions to the acquisition of data.

Conflicts of Interest

The authors have no conflicts of interest to disclose.

Funding

The Dutch Organization for Health Research and Development, Health Care Efficiency Research programme (ZonMw, grant number 171102025) funded the SUPER study.

References

1 Momsen AH, Jensen MB, Norager CB, Madsen MR, Vestersgaard-Andersen T, Lindholt JS. Drug therapy for improving walking distance in intermittent claudication: a systematic review and meta-analysis of robust randomised controlled studies. *Eur J Vasc Endovasc Surg* 2009;**38**:463–74.
2 McDermott MM, Ades P, Guralnik JM, Dyer A, Ferrucci L, Liu K, et al. Treadmill exercise and resistance training in patients with peripheral arterial disease with and without intermittent claudication: a randomized controlled trial. *JAMA* 2009;**301**:165–74.
3 Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG. TASC II working group. Inter-society consensus for the management of peripheral arterial disease (TASC II). *J Vasc Surg* 2007;**45**(Suppl. S):S5–67.
4 Bosch JL, Hunink MG. Meta-analysis of the results of percutaneous transluminal angioplasty and stent placement for aortoiliac occlusive disease. *Radiology* 1997;**204**:87–96.
5 Gardner AW, Poehlman ET. Exercise rehabilitation programs for the treatment of claudication pain. A meta-analysis. *JAMA* 1995;**274**:975–80.
6 Frans FA, Bipat S, Reekers JA, Legemate DA, Koelemay MJ. Systematic review of exercise training or percutaneous transluminal angioplasty for intermittent claudication. *Br J Surg* 2012;**99**:16–28.
7 Bendermacher BL, Willigendael EM, Teijink JA, Prins MH. Supervised exercise therapy versus non-exercise therapy for intermittent claudication. *Cochrane Database Syst Rev* 2006. CD005263.
8 Wind J, Koelemay MJ. Exercise therapy and the additional effect of supervision on exercise therapy in patients with intermittent claudication. Systematic reviews of randomised controlled trials. *Eur J Vasc Endovasc Surg* 2007;**34**:1–9.
9 Spronk S, Bosch JL, den Hoed PT, Veen HF, Pattynama PM, Hunink MG. Intermittent claudication: clinical effectiveness of endovascular revascularization versus supervised hospital-based exercise training–randomized controlled trial. *Radiology* 2009;**250**:586–95.
10 Spronk S, Bosch JL, den Hoed PT, Veen HF, Pattynama PM, Hunink MG. Cost-effectiveness of endovascular revascularization compared to supervised hospital-based exercise training in patients with intermittent claudication: a randomized controlled trial. *J Vasc Surg* 2008;**48**:1472–80.
11 Schulz KF, Altman DG, Moher D, CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010;**340**:c332.
12 World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. [cited 2011 Oct 26] Available from: http://ohsr.od.nih.gov/guidelines/helsinki.html.
13 Nederlands Trial Register [Internet]. Amsterdam: Academic Medical Center (The Netherlands). *Identifier NTR2776. SUPERvised exercise therapy or immediate PTA for intermittent claudication in patients with an iliac artery obstruction: a randomized controlled trial.* SUPER study. 2011 July [cited 2011 July 6]; [1 page]. Available from: http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=2776; 2011 Feb 22.
14 ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). *Identifier: NCT01385774, SUPER Study; SUPERvised exercise or angioplasty for intermittent claudication due to an iliac artery obstruction. 2011 July - [cited 2011 July 6].* Available from: http://clinicaltrials.gov/ct2/show/NCT01385774; 2011 Jun 28.
15 Jongert MWA, Hendriks HJM, Van Hoek J, Klaasboer-Kogelman K, Robeer GG, Simens B, et al. KNGF-richtlijn Claudicatio Intermittens. *NSTD Fysiotherapie* 2003;**6**(Suppl.):3–58.
16 Vahl AC, Reekers JA. Richtlijn 'Diagnostiek en behandeling van arterieel vaatlijden van de onderste extremiteit' van de Nederlandse Vereniging voor Heelkunde. *Ned Tijdschr Geneeskd.* 2005;**149**:1670–4.
17 Tetteroo E, van der Graaf Y, Bosch JL, van Engelen AD, Hunink MG, Eikelboom BC, et al. Randomised comparison of primary stent placement versus primary angioplasty followed by selective stent placement in patients with iliac-artery occlusive disease. Dutch Iliac Stent Trial Study Group. *Lancet* 1998;**351**:1153–9.
18 Stalman WAB, Scheltens T, Smorenburg SM, Hukkelhoven CWPM, Burgers JS. *NHG-Standaard Cardiovasculair risicomanagement 2006* 2006. Utrecht: Nederlandse Huisartsen genootschap.
19 McDermott MM, Criqui MH, Liu K, Guralnik JM, Greenland P, Martin GJ, et al. Lower ankle/brachial index, as calculated by averaging the dorsalis pedis and posterior arterial pressures, and association with leg functioning in peripheral arterial disease. *J Vasc Surg* 2000;**32**:1164–71.
20 Nehler MR, McDermott MM, Treat-Jacobson D, Chetter I, Regensteiner JG. Functional outcomes and quality of life in peripheral arterial disease: current status. *Vasc Med* 2003;**8**:115–26.
21 Nehler MR, Peyton BD. Is revascularization and limb salvage always the treatment for critical limb ischemia? *J Cardiovasc Surg (Torino* 2004;**45**:177–84.
22 Mc Horney CA, Ware JE, Lu JF, Sherbourne CD. The MOS 36 item Short Form Health Survey (SF-36): III. Tests of data quality, scaling assumptions, and reliability across diverse patient groups. *Med Care* 1994;**32**:40–66.
23 Mehta T, Venkata SA, Chetter I, McCollum P. Disease-specific quality of life assessment in intermittent claudication: review. *Eur J Vasc Endovasc Surg* 2003;**25**:202–8.
24 De Vries V, Ouwendijk R, Kessels AG, de Haan MW, Flobbe K, Hunink MG, et al. Comparison of generic and disease-specific questionnaires for the assessment of quality of life in patients with peripheral arterial disease. *J Vasc Surg* 2005;**41**:261–8.
25 Morgan MB, Crayford T, Murin B, Fraser SC. Developing the vascular quality of life questionnaire: a new disease specific quality of life measure for use in lower limb ischemia. *J Vasc Surg* 2001;**33**:679–87.
26 Holman R, Weisscher N, Glas CA, Dijkgraaf MG, Vermeulen M, de Haan RJ, et al. The Academic Medical Center Linear Disability Score (ALDS) item bank: item response theory analysis in a mixed patient population. *Health Qual Life Outcomes* 2005;**3**:83.
27 Met R, Reekers JA, Koelemay MJ, Legemate DA. de Haan RJ.The AMC linear disability score (ALDS): a cross-sectional study with a new generic instrument to measure disability applied to patients with peripheral arterial disease. *Health Qual Life Outcomes* 2009;**7**:88.
28 Frans FA, van Wijngaarden SE, Met R, Koelemay MJW. Validation of the Dutch version of the VascuQol questionnaire and the Amsterdam linear disability score in patients with intermittent claudication. *Qual Life Res* 2011 Nov 15 [Epub ahead of print].
29 Dolan P. Modelling valuations for EuroQol health states. *Med Care* 1997;**35**:1095–108.
30 Lamers LM, Stalmeier PF, McDonnell J, Krabbe PF, van Busschbach JJ. [Measuring quality of life in economic evaluations: the Dutch EQ-5D tariff]. *Ned Tijdschr Geneeskd* 2005;**149**:1574–8.